Development of Watershed Classification Systems for Diagnosis of Biological Impairment in Watersheds and Their Receiving Waterbodies

The U.S. Environmental Protection Agency (EPA) Office of Research and Development is soliciting grant applications for establishing watershed classification schemes in different regions of the United States to support the design of efficient monitoring strategies, diagnose the causes of biological impairment, and prioritize watersheds for restoration activities. This will involve defining both the structural characteristics of a classification strategy (geographic dependence vs. independence, scale, hierarchy, discrimination of natural features from anthropogenic alteration), functional characteristics (theoretical basis for defining categories), and pragmatic aspects of implementation (regional and national relevance, ease of application, flexibility, accuracy, nature of technical transfer products).

In risk assessments, classification schemes serve as an aid for boundary definition in problem formulation and as a tool for extrapolation of exposure–effect relationships in risk characterization. Ultimately, watershed classification systems can serve as 1) the basis for stratification in monitoring strategies to detect responses to nonpoint-source pollution, 2) a tool to assess watershed vulnerability and diagnose potential causes of biological impairment, 3) a method to prioritize watersheds for restoration activities, and 4) a tool to extrapolate results of empirical or mechanistic models of watershed response to other similar watersheds, potentially across entire regions. Classification thus reveals to watershed managers increased opportunities for risk prevention and locally appropriate goals and methods for watershed restoration.

This RFA builds upon earlier Science To Achieve Results grants in aquatic ecosystem classification by exploring relationships between watershed attributes and aquatic ecosystem condition. In addition, this RFA goes beyond the development of methods to assess current condition by addressing the development of methods to assess differences in ecosystem vulnerability to stressors and differences in restoration opportunities within a watershed context. The EPA is interested in building on current classification work by developing the strong underlying basic science that establishes a conceptual understanding of how baseline aquatic ecosystem condition relates to watershed attributes (physical, climatic, terrestrial) and how anthropogenic activity alters baseline conditions. Classification schemes completed through this RFA will enhance the ability of state, tribal, and local agencies to protect the nation's waters.

The outcome of the research will help address these questions: 1) how regionalized watershed classification schemes can be developed within the context of a national framework to determine ecosystem vulnerability and opportunities for watershed restoration; 2) the degree to which ecologically relevant flow-regime metrics, including those describing base-flow and peak-flow conditions, can be predicted based on watershed characteristics; 3) how functional relationships between watershed attributes and hydrological, water quality, and biological responses at different scales can be incorporated into a hierarchical classification scheme to predict regional-, watershed-, and waterbody-scale sensitivities to aquatic nonpoint-source stressors; 4) the degree to which the sensitivity of aquatic ecosystems to the effects of anthropogenic changes to watersheds can be predicted based on the inherent biophysical characteristics of watersheds; 5) the degree to which relationships can be quantified between hydrologic regime and nonpoint-source pollution processes, such as sediment yields, nutrient loadings, aquatic thermal regimes, and riparian and instream habitat structure and quality, in a watershed; and 6) the specific environmental problems that might be amenable to solving with application of the proposed classification scheme.

Successful applications will include development of a regionalized classification scheme and explicit information on how the calibration and validation of the classification scheme would be carried out. The application must also address all of the following attributes of watershed classification frameworks: geographically dependent vs. independent frameworks, scale, hierarchy, regional relevance, relationship to impairment, basis for developing categories, and basis in theory.

Responses to this solicitation must address how classification schemes and response models will be tested, either through analysis of existing data or through collection of new data. Preferably, collection of new data will be linked to existing monitoring programs, through collaboration with local, state, or tribal agencies, watershed managers, or other nonprofit organizations. Applicants must discuss how difficult, expensive, or practical it would be for others, specifically state monitoring programs, to apply the classification methodology themselves. Ideally, watershed classification schemes will rely on the use of readily available GIS data or attributes that can be readily derived from such data so that they can be applied in the near term by public agencies.

Proposals must include a means to assess the level of accuracy associated with their watershed classification system. Applicants are expected to address quality assurance; see the standard instructions for a discussion of the statement required with the proposal. Those proposals recommended for an award will be expected to provide additional detail. Quality assurance documentation will need to address how a classification system will meet proposed data quality objectives for a given quality assurance program plan created by a governmental management entity. This will help facilitate coordination with existing regional, state, and/or tribal monitoring organizations.

Applicants must specifically address how the watershed classification scheme will support more efficient monitoring efforts, improve diagnosis of causes of biological impairment, and/or prioritize watershed restoration efforts. Results of the proposed research must be clearly defined. A clear distinction must be made between outputs and outcomes of the research. Applicable results include 1) a solid and easily applied classification methodology, 2) a classified set of watersheds for a given region, and 3) a database and/or an expert system tool for classification. The primary and essential output will be a classification scheme.

It is anticipated that a total of approximately $4 million will be awarded, depending on the availability of funds. EPA anticipates funding approximately five grants under this RFA. The projected award range is $150,000–300,000 per year ($450,000–900,000 per grant) including direct and indirect costs for up to three years, depending on whether new field data are collected.

More information on this RFA is available online at http://es.epa.gov/ncer/rfa/current/2003wshedclass.html. The deadline for final applications is 29 January 2003. A set of special instructions on how applicants should apply for this grant is available online at http://es.epa.gov/ncer/rfa/forms/. The necessary forms for submitting an application are also provided on this website.

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Mouse Models of Human Cancers Consortium

The National Cancer Institute (NCI) invites new and competing renewal cooperative agreement (U01) and NIH intramural applications from groups of investigators to continue the Mouse Models of Human Cancers Consortium (MMHCC). The scientific scope of this integrative human/mouse cancer research program may be expanded through incorporation of individuals or groups with additional new perspectives and expertise, such as chemistry, computational and mathematical modeling, and systems biology, to create transdisciplinary approaches to the design, analysis, and applications of mouse cancer models.

The intent of the NCI in this RFA is to foster research investigations, technological innovation, and extensive collaboration that cannot be pursued with traditional grant support. Applicants to this RFA are encouraged to propose risky approaches that incorporate broad knowledge of human cancer research into the design, analysis, and applications of mouse cancer models, and to incorporate biocomputational, mathematical modeling, and systems biology strategies to inform design of genetic models and their cross-comparisons to human cancer. The newly implemented transdisciplinary nature of the MMHCC will sustain discoveries that should stimulate mechanistic hypotheses for future research and generate additional tools in support of translational and clinical cancer science.

Significant advances in the science of mouse cancer modeling reflect the rapid acquisition of mouse and human genome sequence information, the informatics tools to analyze and compare them, innovative technologies to derive molecular signatures of human and mouse cancer, and the evolution of new approaches to mouse engineering and phenotyping. As new observations about human cancer biology emerge, additional mouse germline or other engineering approaches may be needed to recapitulate them in mice.

One key emerging use for mouse cancer models is as tools for research on interventions—to define molecular targets and to test molecularly targeted agents for therapy and prevention. Models can be used to illuminate the mechanisms for less-than-optimal clinical experience of a given agent. To explore how to improve clinical outcome, researchers can test new combination therapies in mice; with this strategy, they often find that the mutated genes drive cancer progression by a different mechanism than first hypothesized. Such discoveries can lead to the development of new classes of agents that reflect better knowledge about the function of particular genes in tumors.

Published results of this kind suggest that there are many potential avenues yet to investigate. It will be an essential goal of the MMHCC to apply the most promising cancer models to identify the range of clinical questions for which they are useful. There are many opportunities to invent and test new delivery systems, including those enabled by recent advances in nanotechnology. In addition, mouse cancer models can be used to define the genetic determinants of response or resistance to interventions.

The NCI anticipates that augmenting the mouse cancer modeling expertise of the MMHCC with a broader base of perspectives in the future will enable the consortium to design and generate additional mouse cancer models and modeling strategies, invent new ways and employ existing methods to characterize the models much more fully for cross-comparisons to human cancer, substantially expand the repertoire of applications to many more aspects of human cancer research, and employ bioinformatics to an unprecedented degree to ensure full integration of human and mouse model cancer research.

In this RFA, the NCI encourages applications from groups with broad expertise that may include, but is not limited to, 1) mouse-related research, such as genetics, genetic engineering, biology, physiology, and phenotyping; 2) application of cancer models to human basic, translational, clinical, and population science; 3) application of computational and statistical sciences, mathematical modeling, and bioinformatics to integrate human and mouse cancer research; 4) use of chemistry, genomics, proteomics, imaging, and image analysis to inform model design, characterization, and application; and 5) development of innovative technologies to support derivation, phenotyping, and translational applications of new or existing mouse cancer models.

To implement the MMHCC, the NCI will select as components up to 18 new and competing renewal U01 applications and up to 4 NIH intramural projects, each supporting a multidisciplinary team. Each component will be a self-assembled team of investigators who contributes to the MMHCC effort a unique blend of complementary research experience.

This RFA will use the NIH U01 award mechanism. The anticipated award date is 1 April 2004. NCI intends to commit approximately $18 million in fiscal year 2004 extramural funds to support new and competing renewal grants in response to this RFA.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. The deadline for letters of intent is 19 February 2003, with final applications due 19 March 2003. Complete information on this RFA is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-CA-04-002.html.

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Continued Development and Maintenance of Bioinformatics/Computational Biology Software

Biomedical research laboratories occasionally create software to solve a problem the laboratory faces. These software packages sometimes evolve into a well-designed system that can be easily extended and that is useful to a much broader community beyond the members of the originating laboratory. The goal of this PA is to support the continued development, maintenance, testing, and evaluation of existing software. The proposed work should apply best practices and proven methods for software design, construction, and implementation to extend the applicability of existing bioinformatics–computational biology software to a broader biomedical research community.

This initiative pertains to bioinformatics/computational biology software that is recognized to perform an important function in furthering biomedical research. The software should perform reliably and precisely according to the computing demands of end users. The algorithms that are employed by the software should be well documented, as should be the underlying assumptions of these algorithms to prevent potential misuse.

Contemporary software must be fully documented and easy to modify and extend. Defects that arise in any software must be correctable with limited effort. As the needs of a community of users change, the software that supports their research efforts must be easily modified. Reparability and evolvability are particularly important because the scientific discovery process is open-ended and ever-changing. Interoperability and portability are also a major concern. Where appropriate, software applications should operate on a variety of platforms employing different operating systems.

Awards made under this PA will support continued software development, evaluation, and testing of preexisting bioinformatics/computational biology software for data management and analysis, computational biology, and modeling and simulation. Support will be provided for porting software to new platforms and operating systems as well as the costs associated with maintaining the software as existing operating systems change. The proposed software should not substantially duplicate another software package that is already in wide use.

This PA will use the NIH R01 award mechanism as well as competitive supplements to existing R01, R33, P01, P41, P50, and P60 grants that have already been awarded by one of the participating institutes or centers. Applications for competitive supplements cannot extend beyond the parent project period of performance, and the principal investigator must be the same.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. Applications submitted in response to this PA will be accepted at the standard application deadlines, available at http://grants.nih.gov/grants/dates.htm. Application deadlines are also indicated in the PHS 398 application kit.

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